Expanded-Spectrum ß-lactam Resistance among Human Clinical Enterobacteriaceae in the United States: Results and Characterization of 2000 NARMS Surveillance

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Background: Third-generation cephalosporins are useful for the treatment of invasive salmonellosis and other severe pediatric infections. The National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria has identified increased cephalosporin resistance in human bacterial enteric pathogens; in 1999 1.5% of isolates tested exhibited intermediate or resistant minimum inhibitory concentrations to expanded-spectrum cephalosporins. Preliminary molecular characterization of resistance determinants in the 2000 NARMS collection is presented.

Methods: As NARMS participants, the 17 state and local public health laboratories submitted every 10th non-typhoid *Salmonella*, every 10th *Shigella* and every 5th *E. coli* O157:H7 received in 2000 to the Centers for Disease Control and Prevention for antimicrobial susceptibility testing. Minimum inhibitory concentrations (MIC) were determined for 17 antimicrobials using broth microdilution (Sensititre®). Isolates were chosen for further study based on an intermediate or resistant MIC for the expanded-spectrum cephalosporins: cefoxitin (>=16 µg/ml), ceftiofur (>=4 µg/ml) or ceftriaxone (>=16 µg/ml). ß-lactamases were characterized using isoelectric focusing and pcr for *bla*$_{CMY-2}$.

Results: Of the 2236 isolates tested in 2000, 57 (2%) met the MIC criteria and were selected for further study. These 57 isolates comprised 3% (46/1378) of the non-typhoidal *Salmonella* isolates tested, 2% (7/451) of *Shigella*, and 1% (4/407) of *E. coli* O157:H7. Overall, 52 (91%) of the 57 isolates produced a ß-lactamase with a pI>=8.4, consistent with an ampC-type ß-lactamase. Forty-four (77%) were pcr-positive for a *bla*$_{CMY}$ gene. All 4 *E. coli* O157:H7 isolates tested produced an enzyme with a pI>=8.4 and were also pcr-positive for a *bla*$_{CMY}$ gene. All 7 Shigella isolates tested were S. sonnei and produced an enzyme with a pI>=8.4, but were negative by pcr for *bla*$_{CMY}$. Forty of the 46 Salmonella isolates tested produced an enzyme with a pI>=8.4 and were pcr-positive for a *bla*$_{CMY}$ gene. Notably, 24 of the 40 *bla*$_{CMY}$ positive *Salmonella* were serotype Newport. Seven of the 57 isolates (12%) produced additional ß-lactamases, including 4 *Salmonella* and 3 *Shigella sonnei*. One isolate (*Salmonella* serotype Nienstedten) produced enzymes of pI 5.4 and 8.0.

Conclusions: The presence of isolates exhibiting intermediate or resistant MIC to expanded-spectrum cephalosporins increased in 2000. The major determinant in the 2000 NARMS collection appears to be a *bla*$_{CMY}$-type ß-lactamase. *S*. Newport is the predominant organism among the 2000 NARMS isolates exhibiting this resistance. Additional ß-lactamases are expressed in over 10% of the isolates as well. Because of the pervasive ß-lactam resistance phenotype conferred by the ampC-type enzymes, these additional enzymes would not have been identified by susceptibility testing alone.

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